

## **REMARKS/ARGUMENTS**

### **1. Rejection under 35USC§102(e)**

The Examiner rejected claims 1-16, 23, and 26-31 under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Aoyagi et al. (5,952,202). The rejection is respectfully traversed.

In a previous response sent on May 6, 2003, applicants pointed out that their claimed invention, unlike Aoyagi, teaches the following element of claim 1 of the instant application, “wherein the forward primer and the detectable probe are separated by 0 to 5 nucleotides when hybridized to the external control polynucleotide, or its complement, and the reverse primer and the detectable probe are separated by 0 to 5 nucleotides when hybridized to the external control polynucleotide, or its complement.” Applicants’ argued on May 6, 2003, that since Aoyagi fails to teach this limitation, Aoyagi is not an appropriate 102(e) reference, nor is it an appropriate 103(a) reference.

In the Examiner’s response to the May 6, 2003 response, the Examiner argued that the language “external control” is intended use, and is equivalent to the external control polynucleotide of applicants’ claimed invention, “since they both are polynucleotide used as control polynucleotide in polymerase chain reaction.”

Applicants’ respectfully disagree.

The language “external control” is not intended use. “External control” is an element and limitation of the claimed invention. It is a characteristic of the claimed invention that the external control is in a separate reaction. As Examiner notes “Aoyagi et al., do not disclose the kit which comprises an external control polynucleotide.” Since Aoyagi fails to teach this element, Aoyagi is not an appropriate 102(e) reference. Reconsideration is respectfully requested.

Further, applicants’ claimed invention teaches an external control polynucleotide “wherein the forward primer and the detectable probe are separated by 0 to 5 nucleotides when hybridized to the external control polynucleotide, or its complement, and the reverse primer and the detectable probe are separated by 0 to 5 nucleotides when hybridized to the external control polynucleotide, or its complement.” The separation by 0 to 5 nucleotides of applicants’ claimed invention is not “intended use” as the Examiner suggests, but rather a structural limitation not

taught by Aoyagi. Thus, applicants' maintain that Aoyagi is not an appropriate 102(e) reference. Reconsideration is respectfully requested.

## **2. Rejection under 35USC§103(a)**

The Examiner rejects claims 1-16, 23 and 26-31 under 103(a) over Aoyagi, stating "One of ordinary skill in the art would have been motivated to construct the kit comprising an external control polynucleotide as claimed because as addressed by Aoyagi et al., kits make the practice of a method more reproducible and easier to perform." The rejection is respectfully traversed.

As a first matter, the applicants point out that not all controls are the same. The applicants' claimed invention comprises an *external* control polynucleotide. Such a control provides different information than the internal control taught in Aoyagi. The Examiner has provided no basis for showing that one having ordinary skill in the art would be motivated to remove the internal control polynucleotide taught by Aoyagi and place it in a different reaction. In the absence of establishing this motivation, the Examiner has not met the burden of establishing a prima facie case for obviousness. Thus, applicants' maintain that Aoyagi is not an appropriate 103(a) reference. Reconsideration is respectfully requested.

Further, as discussed supra, Aoyagi does not teach the following element of claim 1 of the instant application, "wherein the forward primer and the detectable probe are separated by 0 to 5 nucleotides when hybridized to the external control polynucleotide, or its complement, and the reverse primer and the detectable probe are separated by 0 to 5 nucleotides when hybridized to the external control polynucleotide, or its complement." In order to establish a prima facie case of obviousness, each element of applicants' claimed invention must be in the cited reference. Since Aoyagi fails to teach or suggest this element, the rejection should be withdrawn.

In summary, the examiner has not established a prima facie case of obviousness regarding Aoyagi. The examiner has not shown motivation by one of skill in the art to use an external control polynucleotide. Specifically, the Examiner has shown no motivation to use the internal control polynucleotide of Aoyagi, in the external reaction of applicants' claimed invention. Further, the Examiner has not shown that Aoyagi teaches each element of applicants'

claimed invention. Specifically, the Examiner has not shown that Aoyagi teaches “wherein the forward primer and the detectable probe are separated by 0 to 5 nucleotides when hybridized to the external control polynucleotide, or its complement, and the reverse primer and the detectable probe are separated by 0 to 5 nucleotides when hybridized to the external control polynucleotide, or its complement.” Since examiner has failed to make a prima facie case of obviousness, reconsideration and removal of the 103(a) rejection is respectfully requested.

### **3. Rejection under 35USC§103(a)**

The Examiner rejects claims 24-25 under 103(a) over Aoyagi, stating *inter alia* that “it would have been prima facie obvious for one of ordinary skill in the art to include one more control polynucleotide in the kit for easier performing the method.” The rejection is respectfully traversed.

As discussed supra, Aoyagi does not teach the following element of claim 1 of the instant application, “wherein the forward primer and the detectable probe are separated by 0 to 5 nucleotides when hybridized to the external control polynucleotide, or its complement, and the reverse primer and the detectable probe are separated by 0 to 5 nucleotides when hybridized to the external control polynucleotide, or its complement.” In order to establish a prima facie case of obviousness, each element of applicants’ claimed invention must be in the cited reference. Since Aoyagi fails to teach or suggest this limitation, the rejection should be withdrawn.

Further, the applicants point out that not all controls are the same. The applicants’ claimed invention comprises an *external* control polynucleotide. Such a control provides different information than the internal control taught in Aoyagi. The Examiner has provided no basis for showing that one having ordinary skill in the art would be motivated to remove the internal control polynucleotide taught by Aoyagi and place it in a different reaction. In the absence of establishing this motivation, the Examiner has not met the burden of establishing a prima facie case for obviousness. Thus, applicants’ maintain that Aoyagi is not an appropriate 103(a) reference. Reconsideration is respectfully requested.

#### **4. Rejection under 35USC§103(a)**

Examiner rejected claims 18-21 under 103(a) over Aoyagi as applied to claims 1-16, 23, and 26-31 above, and further in view of Kutyaivin et al. (5,801,155), stating *inter alia* that “it would have been prima facie obvious for one of ordinary skill in the art to construct a kit including a minor groove binding molecules as claimed.” The rejection is respectfully traversed.

As discussed supra, Aoyagi does not teach the following element of claim 1 of the instant application, “wherein the forward primer and the detectable probe are separated by 0 to 5 nucleotides when hybridized to the external control polynucleotide, or its complement, and the reverse primer and the detectable probe are separated by 0 to 5 nucleotides when hybridized to the external control polynucleotide, or its complement.” Kutyaivin does not rectify this deficiency. In order to establish a prima facie case of obviousness, each element of applicants’ claimed invention must be in the cited reference. Since Aoyagi alone, Kutyaivin alone, or both Aoyagi and Kutyaivin in combination, fail to teach or suggest this limitation, the rejection should be withdrawn.

Further, the applicants point out that not all controls are the same. The applicants’ claimed invention comprises an *external* control polynucleotide. Such a control provides different information than the internal control taught in Aoyagi. The Examiner has provided no basis for showing that one having ordinary skill in the art would be motivated to remove the internal control polynucleotide taught by Aoyagi and place it in a different reaction. Kutyaivin does not rectify this deficiency. In the absence of establishing this motivation, the Examiner has not met the burden of establishing a prima facie case for obviousness. Thus, applicants’ maintain that Aoyagi in light of Ktyavin are not appropriate 103(a) references. Reconsideration is respectfully requested.

#### **5. Rejection under 35USC§103(a)**

Examiner rejected claim 17 under 103(a) over Aoyagi as applied to claims 1-16, 23, and 26-31 above, and further in view of Livak et al. (5,538,848) stating *inter alia* that “it would have been prima facie obvious for one of ordinary skill in the art to construct a kit including a

quencher which is non-fluorescence as needed as claimed.” The rejection is respectfully traversed.

As discussed supra, Aoyagi does not teach the following element of claim 1 of the instant application, “wherein the forward primer and the detectable probe are separated by 0 to 5 nucleotides when hybridized to the external control polynucleotide, or its complement, and the reverse primer and the detectable probe are separated by 0 to 5 nucleotides when hybridized to the external control polynucleotide, or its complement.” Livak does not rectify this deficiency. In order to establish a prima facie case of obviousness, each element of applicants’ claimed invention must be in the cited reference. Since Aoyagi alone, Livak alone, or both Aoyagi and Livak in combination, fail to teach or suggest this limitation, the rejection should be withdrawn.

Further, the applicants point out that not all controls are the same. The applicants’ claimed invention comprises an *external* control polynucleotide. Such a control provides different information than the internal control taught in Aoyagi. The Examiner has provided no basis for showing that one having ordinary skill in the art would be motivated to remove the internal control polynucleotide taught by Aoyagi and place it in a different reaction. Livak does not rectify this deficiency. In the absence of establishing this motivation, the Examiner has not met the burden of establishing a prima facie case for obviousness. Thus, applicants’ maintain that Aoyagi in light of Livak are not appropriate 103(a) references. Reconsideration is respectfully requested.

## **6. Rejection under 35USC§103(a)**

Examiner rejected claim 22 under 103(a) over Aoyagi as applied to claims 1-16, 23, and 26-31 above, and further in view of Williams et al. (6,232,075) stating *inter alia* that “it would have been prima facie obvious for one of ordinary skill in the art at the time of the instant invention to include the nucleotide 5’-triphosphates comprising a fluorescent dye in the kit as claimed.” The rejection is respectfully traversed.

As discussed supra, Aoyagi does not teach the following element of claim 1 of the instant application, “wherein the forward primer and the detectable probe are separated by 0 to 5 nucleotides when hybridized to the external control polynucleotide, or its complement, and the

reverse primer and the detectable probe are separated by 0 to 5 nucleotides when hybridized to the external control polynucleotide, or its complement.” Williams does not rectify this deficiency. In order to establish a prima facie case of obviousness, each element of applicants’ claimed invention must be in the cited reference. Since Aoyagi alone, Williams alone, or both Aoyagi and Williams in combination, fail to teach or suggest this limitation, the rejection should be withdrawn.

Further, the applicants point out that not all controls are the same. The applicants’ claimed invention comprises an *external* control polynucleotide. Such a control provides different information than the internal control taught in Aoyagi. The Examiner has provided no basis for showing that one having ordinary skill in the art would be motivated to remove the internal control polynucleotide taught by Aoyagi and place it in a different reaction. Williams does not rectify this deficiency. In the absence of establishing this motivation, the Examiner has not met the burden of establishing a prima facie case for obviousness. Thus, applicants’ maintain that Aoyagi in light of Williams are not appropriate 103(a) references. Reconsideration is respectfully requested.


Applicants believe the above remarks and arguments place the application in condition for allowance, and look forward to allowance of the claims as written.

**FEE AUTHORIZATION and REQUEST FOR TIME EXTENSION**

A Petition for a 3-Month Extension of Time is enclosed herewith. If any additional time extensions are required, such time extensions are hereby requested. If any additional fees not submitted with this response are required, please take such fees from Applied Biosystems Deposit Account No. 01-2213 (Order No. 4498C1).

Respectfully submitted,

Date: 1-29-04

  
Andrew K. Finn  
Agent for Applicants  
Reg. No. 54,097  
Telephone: 650-554-3392

**CORRESPONDENCE ADDRESS**

Customer Number 22896  
Applied Biosystems Group  
850 Lincoln Centre Drive M/S 432-2  
Foster City, California 94404  
TEL: 650-554-3392  
FAX: 650-638-6677